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Fraden et al.

(54) MANIPULATION OF FLUIDS, FLUID COMPONENTS AND REACTIONS IN MICROFLUIDIC SYSTEMS

(75) Inventors: Seth Fraden, Newton, MA (US); Hakim

Boukellal, Paris (FR); Yanwei Jia, Medford, MA (US); Seila Selimovic, Bronx, NY (US); Amy Rowat,

Cambridge, MA (US); Jeremy Agresti, Cambridge, MA (US); David A. Weitz,

Bolton, MA (US)

(73) Assignees: Brandeis University; President and

Fellows of Harvard College

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See application file for complete search history.

(56) References Cited

U.S. PATENT DOCUMENTS

2,097,692 A 11/1937 Fiegel 2,164,172 A 6/1939 Dalton (Continued)

FOREIGN PATENT DOCUMENTS

AU 2004225691 B2 10/2004 CA 2520548 A1 9/2004

(Continued)

OTHER PUBLICATIONS

Adang, A.E. et al., The contribution of combinatorial chemistry to lead generation: an interim analysis, Curr Med Chem 8: 985-998 (2001)

(Continued)

Primary Examiner — Paul Hyun (74) Attorney, Agent, or Firm — Brown Rudnick LLP; Thomas C. Meyers

(57) ABSTRACT

Microfluidic structures and methods for manipulating fluids, fluid components, and reactions are provided. In one aspect, such structures and methods can allow production of droplets of a precise volume, which can be stored/maintained at precise regions of the device. In another aspect, microfluidic structures and methods described herein are designed for containing and positioning components in an arrangement such that the components can be manipulated and then tracked even after manipulation. For example, cells may be constrained in an arrangement in microfluidic structures described herein to facilitate tracking during their growth and/or after they multiply.

26 Claims, 27 Drawing Sheets

